

CLAIMS

What is claimed is:

SUB A1
5 1. A method of treating a mammalian subject to prevent stenosis or restenosis of a blood vessel, comprising the step of:
administering to a mammalian subject in need of treatment to prevent stenosis or restenosis of a blood vessel a composition comprising a polynucleotide, said polynucleotide comprising a nucleotide sequence that encodes a vascular endothelial growth factor C (VEGF-C) polypeptide, thereby preventing stenosis or restenosis of said blood vessel.

10 2. A method according to claim 1 wherein said mammalian subject is human.

3. A method according to claim 2 wherein said VEGF-C polypeptide comprises a mammalian VEGF-C.

4. A method according to claim 2 wherein said VEGF-C polypeptide comprises a human VEGF-C.

15 5. A method according to claim 2 wherein said VEGF-C polypeptide comprises an amino acid sequence comprising a continuous portion of SEQ ID NO: 2, said continuous portion having, as its amino terminus, an amino acid selected from the group consisting of positions 30-131 of SEQ ID NO: 2, and having, as its carboxyl terminus, an amino acid selected from the group consisting of positions 211 to 419 of SEQ ID NO: 2.

20 6. A method according to claim 5 wherein said polynucleotide further comprises a nucleotide sequence encoding a secretory-signal peptide, and wherein the sequence encoding the secretory signal peptide is connected in-frame with the sequence that encodes the VEGF-C polypeptide

25 7. A method according to claim 6 wherein said polynucleotide lacks a nucleotide sequence encoding amino acids 228-419 of SEQ ID NO: 2.

8. A method according to claim 7 wherein said polynucleotide lacks a nucleotide sequence encoding amino acids 32-102 of SEQ ID NO: 2.

9. A method according to claim 6 wherein the polynucleotide further comprises a promoter sequence operably connected to the sequence that encodes the secretory signal sequence and VEGF-C polypeptide, wherein the promoter sequence promotes transcription of the sequence that encodes the secretory signal sequence and the VEGF-C polypeptide in cells of the mammalian subject.

10. A method according to claim 9 wherein the polynucleotide further comprises a polyadenylation sequence operably connected to the sequence that encodes the VEGF-C polypeptide.

11. A method according to claim 2 wherein the composition further comprises a pharmaceutically acceptable carrier.

12. A method according to claim 2 wherein the composition comprises a gene therapy vector, said gene therapy vector comprising said polynucleotide.

13. A method according to claim 12 wherein said vector comprises a replication-deficient adenovirus, said adenovirus comprising the polynucleotide operably connected to a promoter and flanked by adenoviral polynucleotide sequences.

14. A method according to claim 2 wherein said administering comprises at least one intravascular injection of said composition.

15. A method according to claim 2 wherein said administering comprises a catheter-mediated transfer of said composition into a blood vessel of the mammalian subject.

SUB
P2
SECRET
109909
SUB
A3

16. A method according to claim 15 wherein said catheter-mediated gene transfer comprises introducing a catheter into a coronary artery of the mammalian subject, and releasing the composition into the coronary artery.

17. A method according to claim 2 wherein said administering is conducted in said human concurrently with a percutaneous transluminal coronary angioplasty.

18. A treatment to prevent stenosis or restenosis of a blood vessel in a human, comprising delivering a replication-deficient adenovirus vector to the vessel, said vector comprising a polynucleotide encoding a VEGF-C polypeptide, and further comprising a promoter sequence to promote expression of the VEGF-C polypeptide in cells of the blood vessel, thereby preventing stenosis or restenosis of the blood vessel.

19. A method of treating a mammalian subject to prevent stenosis or restenosis of a blood vessel, comprising the step of:
administering to a mammalian subject in need of treatment to prevent stenosis or restenosis of a blood vessel a composition comprising a vascular endothelial growth factor C (VEGF-C) polypeptide in an amount effective to prevent stenosis or restenosis of said blood vessel.

20. A method according to claim 19 wherein said administering comprises implanting an intravascular stent in said mammalian subject, and wherein the stent is coated or impregnated with the composition.

21. A method of treating a mammalian subject to prevent stenosis or restenosis of a blood vessel, comprising the step of:
administering to a mammalian subject in need of treatment to prevent stenosis or restenosis of a blood vessel a composition, said composition comprising an anti-restenosis agent selected from the group consisting of Vascular Endothelial Growth Factor D (VEGF-D) polynucleotides and polypeptides, thereby preventing stenosis or restenosis of said blood vessel.

0943757 : 103699
669207 : 292460

SUB
A4

SUB
A5

- SUB
AS
CONT.
22. In a medical device designed to contact a surface of a blood vessel in the course of surgery to treat stenosis of the blood vessel, the improvement comprising integrating into the device a composition effective to prevent restenosis, said composition comprising at least one anti-restenosis agent selected from the group consisting of a VEGF-C polynucleotide, a VEGF-C polypeptide, a VEGF-D polynucleotide, and a VEGF-D polypeptide.

23. The improvement of claim 22, wherein the device is selected from the group consisting of intravascular stents, intravascular catheters, and combinations thereof.

24. The improvement of claim 22, wherein the device comprises an
10 extravascular collar.

25. The improvement of claim 22, wherein the device comprises an elastomeric membrane adapted to cover a surface of an intravascular stent or catheter.

- SUB
AS
CONT.
26. A medical device comprising an endovascular stent having an outer surface for contacting a surface of a blood vessel, and a composition on said surface, said
15 composition comprising at least one anti-restenosis agent selected from the group consisting of a VEGF-C polynucleotide, a VEGF-C polypeptide, a VEGF-D polynucleotide, and a VEGF-D polypeptide.

- SUB
AS
27. A medical device comprising a catheter having an outer surface for contacting a surface of a blood vessel, and a composition on said surface, said composition
20 comprising at least one member selected from the group consisting of a VEGF-C polynucleotide, a VEGF-C polypeptide, a VEGF-D polynucleotide, and a VEGF-D polypeptide.

✓
SUB
A6
CONT.
5 28. A medical device comprising a balloon catheter having a void for holding a therapeutic agent for delivery to the interior of a blood vessel, and a composition contained in the void, the composition comprising at least one anti-restenosis agent selected from the group consisting of a VEGF-C polynucleotide, a VEGF-C polypeptide, a VEGF-D polynucleotide, and a VEGF-D polypeptide.

✓
29. A kit for treating restenosis comprising a container holding at least one anti-restenosis agent selected from the group consisting of a VEGF-C polynucleotide, a VEGF-C polypeptide, a VEGF-D polynucleotide, and a VEGF-D polypeptide; and a label attached to or packaged with the container, the label describing use of the compound for
10 prevention of restenosis of a blood vessel.

30. A kit according to claim 29, further comprising a medical device selected from the group consisting of: intravascular stents, intravascular catheters, extravascular collars, and membranes adapted to cover a surface of an intravascular stent or catheter.

ADD
A7

add
BS

addco

563210